AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

1. (Currently Amended) A sterile, stable nanoparticulate dispersion comprising:

(a) a liquid dispersion medium;

(b) nanoparticulate beclomethasone particles, nanoparticulate budesonide particles, or a combination thereof dispersed in the dispersion medium, the nanoparticulate beclomethasone and nanoparticulate budesonide particles having an effective average particle size of less than 150 nm;

(c) tyloxapol as a surface stabilizer adsorbed onto the surface of the nanoparticulate beclomethasone and/or the nanoparticulate budesonide particles in an amount effective to prevent the aggregation of the nanoparticulate beclomethasone and/or budesonide particles; and

(d) optionally, at least one secondary surface stabilizer adsorbed onto the surface of the nanoparticulate beclomethasone and/or the nanoparticulate budesonide particles,

wherein the nanoparticulate dispersion is free from biological contaminants by sterile ~~filtered~~ filtration with a filter having a pore size of 0.2 μm or less.

2. (Previously Presented) The dispersion of claim 1, wherein the nanoparticulate beclomethasone particles, the nanoparticulate budesonide particles, or the combination thereof are present in an amount selected from the group consisting of about 99% to about 1% (w/w), about 90% to about 10% (w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

3. (Previously Presented) The dispersion of claim 1, wherein the concentration of tyloxapol is selected from the group consisting of from about 0.01 to about 90%, from about 1 to about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight, based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

4. (Previously Presented) The dispersion of claim 1, wherein the effective average particle size of the nanoparticulate beclomethasone particles, the nanoparticulate budesonide particles, or the combination thereof is less than 120 nm.

5. (Previously Presented) The dispersion of claim 1 wherein the effective average particle size of the nanoparticulate beclomethasone particles, the nanoparticulate budesonide particles, or the combination thereof is less than 100 nm.

6. (Previously Presented) The dispersion of claim 1 wherein the effective average particle size of the nanoparticulate beclomethasone particles, the nanoparticulate budesonide particles, or the combination thereof is less than 80 nm.

7. (Previously Presented) The dispersion of claim 1 wherein the effective average particle size of the nanoparticulate beclomethasone particles, the nanoparticulate budesonide particles, or the combination thereof is less than 50 nm.

8. (Cancelled).

9. (Previously Presented) The dispersion of claim 1, wherein the secondary surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid,

sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), $C_{18}H_{37}CH_2(CON(CH_3)\text{-}CH_2(CHOH)_4(CH_20H)_2$, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

10. (Previously Presented) The dispersion of claim 1, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidine.

11. (Previously Presented) The dispersion of claim 1, wherein the nanoparticulate beclomethasone particles and/or the nanoparticulate budesonide particles are crystalline, semi-crystalline, or amorphous.

12. (Cancelled)

13. (Previously Presented) The dispersion of claim 1, wherein the nanoparticulate beclomethasone is in the chemical form of beclomethasone dipropionate.

14. (Previously Presented) The dispersion of claim 1 formulated into an aerosol for nasal or pulmonary administration.

15. (Withdrawn – Currently Amended) A method of making a nanoparticulate composition comprising:

(a) dispersing particles of budesonide, beclomethasone, or a mixture thereof in a liquid dispersion medium; and

(b) applying mechanical means in the presence of grinding media to reduce the average particle size of budesonide, beclomethasone, or a mixture thereof in the liquid dispersion medium to less than about 150 nm, and

(c) sterile filtering the resulting nanoparticulate dispersion through a filter having a pore size of 0.2 μm or less rendering the dispersion free from biological contaminants; wherein tyloxapol is added to the liquid dispersion medium before or after milling, but before sterile filtering.

16. (Withdrawn) The method of claim 15, wherein the beclomethasone particles, budesonide particles, or a combination thereof are present in an amount selected from the group consisting of about 99% to about 1% (w/w), about 90% to about 10% (w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

17. (Withdrawn) The method of claim 15, wherein the concentration of tyloxapol is selected from the group consisting of from about 0.01 to about 90%, from about 1 to about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight, based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

18. (Withdrawn) The method of claim 15, wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is selected from the group consisting of less than about 120 nm, less than about 100 nm, less than about 80 nm, and less than about 50 nm.

19. (Withdrawn) The method of claim 15 further comprising adding at least one secondary surface stabilizer to the liquid dispersion medium before or after milling.

20. (Withdrawn) The method of claim 19, wherein the secondary surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides, dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride,

calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), $C_{18}H_{37}CH_2(CON(CH_3)\text{-}CH_2(CHOH)_4(CH_20H)_2$, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

21. (Withdrawn) The method of claim 19, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidine.

22. (Withdrawn – Previously Presented) The method of claim 15, wherein the beclomethasone and/or budesonide particles are crystalline, semi-crystalline, or amorphous.

23. (Withdrawn – Previously Presented) A method of making a nanoparticulate composition comprising:

(a) dissolving beclomethasone, budesonide, or a combination thereof in a solvent;

(b) adding the solubilized beclomethasone, budesonide, or a combination thereof to a solution comprising tyloxapol to form a clear solution;

(c) precipitating the solubilized beclomethasone, budesonide, or a combination thereof having tyloxapol adsorbed on the surface thereof using a non-solvent; and

(d) sterile filtering the resulting nanoparticulate dispersion through a filter having a pore size of 0.2 μm or less,

wherein the resulting composition of nanoparticulate beclomethasone, budesonide, or a combination thereof has an effective average particle size of less than about 150 nm.

24. (Withdrawn) The method of claim 23, wherein the beclomethasone particles, budesonide particles, or a combination thereof are present in an amount selected from the group consisting of about 99% to about 1% (w/w), about 90% to about 10% (w/w), about 80% to about 30%, and about 80% to about 40% (w/w), based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

25. (Withdrawn) The method of claim 23, wherein the concentration of tyloxapol is selected from the group consisting of from about 0.01 to about 90%, from about 1 to about 75%, from about 10 to about 60%, and from about 10 to about 30% by weight, based on the total combined dry weight of beclomethasone, budesonide, and tyloxapol.

26. (Withdrawn) The method of claim 23, wherein the effective average particle size of the beclomethasone particles, budesonide particles, or a combination thereof is selected from the group consisting of less than about 120 nm, less than about 100 nm, less than about 80 nm, and less than about 50 nm.

27. (Withdrawn) The method of claim 23 further comprising adding at least one secondary surface stabilizer to the liquid dispersion medium before or after milling.

28. (Withdrawn) The method of claim 27, wherein the secondary surface stabilizer is selected from the group consisting of cetyl pyridinium chloride, gelatin, casein, phosphatides,

dextran, glycerol, gum acacia, cholesterol, tragacanth, stearic acid, benzalkonium chloride, calcium stearate, glycerol monostearate, cetostearyl alcohol, cetomacrogol emulsifying wax, sorbitan esters, polyoxyethylene alkyl ethers, polyoxyethylene castor oil derivatives, polyoxyethylene sorbitan fatty acid esters, polyethylene glycols, dodecyl trimethyl ammonium bromide, polyoxyethylene stearates, colloidal silicon dioxide, phosphates, sodium dodecylsulfate, carboxymethylcellulose calcium, hydroxypropyl celluloses, hydroxypropyl methylcellulose, carboxymethylcellulose sodium, methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate, noncrystalline cellulose, magnesium aluminum silicate, triethanolamine, polyvinyl alcohol, polyvinylpyrrolidone, poloxamers, poloxamines, charged phospholipids, dioctylsulfosuccinate, Tetronic 1508®, dialkylesters of sodium sulfosuccinic acid, sodium lauryl sulfates, alkyl aryl polyether sulfonates, mixtures of sucrose stearate and sucrose distearate, p-isononylphenoxypoly-(glycidol), $C_{18}H_{37}CH_2(CON(CH_3)\text{-}CH_2(CHOH)_4(CH_20H)_2$, decanoyl-N-methylglucamide, n-decyl β-D-glucopyranoside, n-decyl β-D-maltopyranoside, n-dodecyl β-D-glucopyranoside, n-dodecyl β-D-maltoside, heptanoyl-N-methylglucamide, n-heptyl-β-D-glucopyranoside, n-heptyl β-D-thioglucoside, n-hexyl β-D-glucopyranoside, nonanoyl-N-methylglucamide, n-noyl β-D-glucopyranoside, octanoyl-N-methylglucamide, n-octyl-β-D-glucopyranoside, octyl β-D-thioglucopyranoside, and random copolymers of vinyl acetate and vinyl pyrrolidone.

29. (Withdrawn) The method of claim 27, wherein the secondary surface stabilizer is selected from the group consisting of dioctylsulfosuccinate, sodium lauryl sulfate, hydroxypropylmethyl cellulose, benzalkonium chloride, and polyvinylpyrrolidine.

30. (Withdrawn – Previously Presented) The method of claim 23, wherein the beclomethasone and/or budesonide particles are crystalline, semi-crystalline, or amorphous.

31. (Withdrawn – Previously Presented) A method of treating a patient in need with a nanoparticulate composition comprising administering to a patient in need a therapeutically

effective amount of a nanoparticulate composition of budesonide, beclomethasone, or a combination thereof, wherein said composition comprises:

(a) budesonide, beclomethasone, or a combination thereof having an effective average particle size of less than about 150 nm; and

(b) tyloxapol adsorbed on the surface of the budesonide and/or beclomethasone, wherein the nanoparticulate composition has been sterile filtered by passing through a filter having a pore size of 0.2 μm or less.

32. (Withdrawn) The method of claim 31, wherein said treatment is for an inflammatory disease.

33. (Withdrawn) The method of claim 31, wherein said treatment is for asthma, cystic fibrosis, or chronic obstructive pulmonary disease.

34. (Withdrawn) The method of claim 31, wherein said composition is administered via a nasal or pulmonary aerosol.

35. (Currently Amended) A sterile nanoparticulate dispersion consisting of:

~~(a) a liquid dispersion medium;~~

~~(b)~~ (a) nanoparticulate beclomethasone particles, nanoparticulate budesonide particles, or a combination thereof ~~dispersed in the dispersion medium~~, the nanoparticulate beclomethasone and nanoparticulate budesonide particles having an effective average particle size of less than 150 nm; and

~~(c)~~ (b) tyloxapol as a surface stabilizer adsorbed onto the surface of the nanoparticulate beclomethasone and/or the nanoparticulate budesonide particles in an amount effective to prevent the aggregation of the nanoparticulate beclomethasone and/or budesonide particles,

wherein the sterile nanoparticulate dispersion is free from biological contaminants.

36. (Currently Amended) A sterile nanoparticulate dispersion produced by a process comprising the steps of:

(a) dispersing particles of budesonide, beclomethasone, or a mixture thereof in a liquid dispersion medium; and

(b) applying mechanical means in the presence of grinding media to reduce the average particle size of budesonide, beclomethasone, or a mixture thereof in the liquid dispersion medium to less than 150 nm, and

(c) sterile filtering the resulting nanoparticulate dispersion through a filter having a pore size of 0.2 μm or less;

wherein the sterile nanoparticulate dispersion is free from biological contaminants, and

wherein tyloxapol is added to the liquid dispersion medium before or after milling.

37. (Currently Amended) A sterile nanoparticulate dispersion produced by a process comprising the steps of:

(a) dissolving beclomethasone, budesonide, or a combination thereof in a solvent;

(b) adding the solubilized beclomethasone, budesonide, or a combination thereof to a solution comprising tyloxapol to form a clear solution;

(c) precipitating the solubilized beclomethasone, budesonide, or a combination thereof having tyloxapol adsorbed on the surface thereof using a non-solvent; and

(d) removing biological contaminants from the dispersion by sterile filtering the resulting nanoparticulate dispersion through a filter having a pore size of 0.2 μm or less,

wherein the resulting composition of nanoparticulate beclomethasone, budesonide, or a combination thereof has an effective average particle size of less than 150 nm.